REMARKS

The claims have been amended to simply prosecution and in accordance with the requirement for restriction. Claims to the non-elected invention, claims 36-67 have been cancelled. Also, canceled are certain claims which gave rise to the requirement for species election-*i.e.*, claims 9-12 and 27-30. Claims to various ligands formerly claims 5 and 23 have been canceled and replaced with claims 68 and 70. It appeared to applicants that not all of the elements in claims 5 and 23 were at the same level-*e.g.*, an antibody would be a polypeptide and an aptamer is a nucleic acid. Applicants elect to pursue the species of ligand which is at least a portion of an antibody as set forth in claims 69 and 71. All claims read on this election.

Applicants have canceled claims that include various active agents and various imaging agents because applicants are of the view that the particulars of these claims distract from the focus of the invention. Applicants do not rely on these specific embodiments for patentability. Accordingly, these claims have been canceled. Applicants are unclear with regard to the specification of "various non-gaseous acoustic substances" (claims 10, 26 and 46) as these claims do not relate to various non-gaseous acoustics imaging substances; claim 10 relates to various materials that are added to the non-gaseous acoustic imaging substance as the claim then read. Claim 26 appears to relate to biologically active agents in general and claim 46 is similar to claims 10.

It will be noted that claims 1 and 18, the only independent claims have been reworded to focus on the administration of liquid fluorocarbons used herein as the acoustic imaging substances. Support for the limitation to fluorocarbon containing emulsions is found in previously pending claims 2 and 20 which have been canceled; support for the limitation to nanoparticles is found, for example, on page 8 of the specification lines 17-22, and throughout the specification. Support for the lipid surfactant encapsulation of these particles is found, for

example, on page 8 of the specification lines 25-26, page 9, lines 18-29, page 10, lines 5-11, page 11, line 2, page 11, lines 26 to page 12 line 14, and throughout the specification. Support for a ligand incorporated into the lipid surfactant capsule is found on page 14 beginning at line 14. Support for the embodiments of ligands is found in former claims 5 and 23. No new matter has been added and entry of the amendment is respectfully requested.

It is believed the claims as amended more directly point out the nature of the invention. Election of a particular biologically active agent and of a particular additional imaging substance is no longer required in view of the cancellation of the relevant claims. Applicants have elected a species of targeting ligand.

The claims have further been modified to clarify that the change in temperature occurs in the administered bound emulsion and the change in reflectivity of the target is thus accomplished. The claims which remain pending are claims 1, 3, 7-8, 13-19, 21, 25-26, 31-35 and 68-71.

In the unlikely event that the transmittal letter is separated from this document and the Patent Office determines that an extension and/or other relief is required, applicants petition for any required relief including extensions of time and authorize the Assistant Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to **Deposit Account No. 03-1952** referencing docket No. 532512000500.

Respectfully submitted,

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EXHIBIT A. - VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the Claims:

1. (Amended) A method for changing acoustic reflectivity of an ultrasound target, the method comprising (1) administering to the target, a nongaseous emulsion comprising nanoparticles that comprise a liquid fluorocarbon which binds to the target and produces a change in acoustic reflectivity with a change in temperature and (2) changing the temperature of the bound emulsion to produce a measurable change in acoustic reflectivity of the target.

3. (Amended) The method according to claim [5]1 wherein the fluorocarbon is perfluorooctane.

7. (Amended) The method according to claim [5]1 wherein the nanoparticles are encapsulated with a lipid surfactant which comprises a ligand that binds to said target.

13. (Amended) The method according to claim 1 wherein changing the temperature comprises energizing the bound [substance] emulsion to increase temperature of the bound emulsion and enhance acoustic reflectivity of the target.

15. (Amended) The method according to claim 1 wherein changing the [of the bound] temperature comprises reducing the temperature of the bound [substance] emulsion to produce a measurable decrease in acoustic reflectivity of the target.

16. (Amended) The method according to 15 wherein reducing the temperature [of the bound] is performed as part of cryotherapy or heart bypass surgery.

17. (Amended) The method according to claim 1 wherein changing the temperature comprises changing the temperature of the bound [substance] emulsion by at least 5°C.

18. (Twice Amended) A method for measuring enhanced acoustic reflectivity of an ultrasound target, the method comprising (1) administering to the target, a nongaseous emulsion

comprising nanoparticles that comprise a liquid fluorocarbon which binds to the target and produces a change in acoustic reflectivity with a change in temperature and (2) changing the temperature of the bound emulsion to produce a measurable change in acoustic reflectivity of the target, and (3) detecting change in acoustic reflectivity of the [bound substance] target.

19. (Amended) The method according to claim 18 wherein detecting comprises (a) measuring reflectivity prior to changing the temperature of the bound [substance] emulsion; (b) measuring reflectivity after changing the temperature of the [substance] emulsion; and (c) determining the change in reflectivity after changing the temperature of the bound emulsion compared to reflectivity prior to changing the temperature of the bound [substance] emulsion.

21. (Amended) The method according to claim [20] 18 wherein the fluorocarbon is perfluorooctane.

25. (Amended) The method according to claim 1[9]8 wherein the nanoparticles are encapsulated with a lipid surfactant which comprises a ligand that binds to said target.

26. (Amended) The method according to claim 1[9]8 wherein the emulsion further comprises a biologically active agent.

31. (Amended) The method according to claim 1[9]8 wherein changing the temperature comprises energizing the bound [substance] emulsion to increase temperature of the bound [substance] emulsion and enhance acoustic reflectivity of the [surface] target.

33. (Amended) The method according to claim 19 wherein changing the temperature of the bound [substance] emulsion comprises reducing the temperature of the bound [substance] emulsion to produce a measurable decrease in acoustic reflectivity of the target.

34. (Amended) The method according to 33 wherein reducing the temperature [of the bound substance] is performed as part of cryotherapy or heart bypass surgery.

35. (Amended) The method according to claim 1[9]8 wherein changing the temperature comprises changing the temperature of the bound emulsion by at least 5°C.